

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/011683

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/72 C12N15/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, Sequence Search, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| X | SUN JUN ET AL: "Molecular basis for the subtype discrimination of the estrogen receptor-beta-selective ligand, diarylpropionitrile." MOLECULAR ENDOCRINOLOGY, vol. 17, no. 2, February 2003 (2003-02), pages 247-258, XP002318377 ISSN: 0888-8809 | 1-4, 11 |
| Y | page 247, left-hand column, paragraph 3 - right-hand column, paragraph 2; figure 2 ----- -/-- | 12, 14, 16, 17, 19, 20 |

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

18 February 2005

Date of mailing of the international search report

19. 05. 2005

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| X | MUELLER STEFAN O ET AL: "Molecular determinants of the stereoselectivity of agonist activity of estrogen receptors (ER) alpha and beta." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 278, no. 14, 4 April 2003 (2003-04-04), pages 12255-12262, XP002318378 ISSN: 0021-9258 | 1-4, 11 |
| Y | page 12257, right-hand column, paragraph 3 - page 12259, left-hand column, paragraph 1; figures 3,4 | 12, 14, 16, 17, 19, 20 |
| Y | ----- WO 02/097050 A (NOVARTIS AG; BRACKEN, KATHRYN, RENE; DE LOS ANGELES, JOSEPH, E; HUANG,) 5 December 2002 (2002-12-05) page 6, paragraph 1 - page 13, paragraph 5 ----- | 1-4, 11, 12, 14-17, 19, 20 |
| Y | WO 98/18925 A (GENEMEDICINE, INC; BAYLOR COLLEGE OF MEDICINE; O'MALLEY, BERT; TSAI, M) 7 May 1998 (1998-05-07) examples 1-10 ----- | 1-4, 11, 12, 14-17, 19, 20 |
| Y | WO 02/28175 A (ASSOCIATION POUR LE DEVELOPPEMENT DE LA RECHERCHE) 11 April 2002 (2002-04-11) page 7, line 3 - page 8, line 2 ----- | 1-4, 11, 12, 14-17, 19, 20 |
| Y | WO 98/05754 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; CITY OF HOPE) 12 February 1998 (1998-02-12) page 5 - page 6; figure 2 ----- | 1-4, 11, 12, 14-17, 19, 20 |
| Y | WO 01/42307 A (SUMITOMO CHEMICAL COMPANY, LIMITED; SAITO, KOICHI; OHE, NORIHISA; SATO) 14 June 2001 (2001-06-14) page 2, paragraph 2 page 5, paragraph 1 - page 6, paragraph 1 ----- | 1-4, 11, 12, 14-17, 19, 20 |
| Y | WO 99/50658 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; ARCH DEVELOPMENT CORPORAT) 7 October 1999 (1999-10-07) page 12, line 30 - page 13, line 16 ----- -/-- | 1-4, 11, 12, 14-17, 19, 20 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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| A | WANG Y ET AL: "A regulatory system for use in gene transfer" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 91, August 1994 (1994-08), pages 8180-8184, XP002121654 ISSN: 0027-8424 cited in the application Introduction, Discussion ----- | 1-4,11, 12, 14-17, 19,20 |
| A | US 6 528 276 B1 (GERMANN URSULA ET AL) 4 March 2003 (2003-03-04) column 5, line 65 - column 6, line 43 column 7, line 65 - column 8, line 20 column 13, line 5 - line 62 ----- | 1-4,11, 12, 14-17, 19,20 |
| A | WO 01/30843 A (NOVARTIS AG; THE SCRIPPS RESEARCH INSTITUTE) 3 May 2001 (2001-05-03) page 4, line 23 - page 6, line 30 ----- | 1-4,11, 12, 14-17, 19,20 |

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 21 (partially)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-4, 11, 12, 14-17, 19, 20 (all partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-4,11,12,14-17,19,20 (all partially)

A polypeptide comprising a modified ligand binding domain of hER-alpha, a transcription factor comprising the same, a polynucleotide encoding the same, a host cell comprising said polynucleotide, an orthogonal gene switch comprising said transcription factor and a vector comprising a target gene fused to a regulatory domain which is recognised by the transcription factor, said switch further comprising a ligand, a method for making such a gene switch comprising creating a library of transcription factors containing modified ligand binding domains and screening inactive ligand analogues for the ability to activate the modified transcription factors and wherein the polypeptide comprises SEQ ID NO. 2.

2. claims: 1-3,5,6,11,12,14-17,19,20 (all partially)

As Invention 1, but with regard to SEQ ID NOs. 3-15.

3. claims: 1-3,7,8,11-17,19,20,23-25 (all partially)

As Invention 1, but having regard to SEQ ID NOs. 16-28.

4. claims: 1-3,9-20,23,24,26 (all partially)

As Invention 1, but having regard to SEQ ID NOs. 29-41 and 43.

5. claims: 27,28,30,32-39

A method of making an orthogonal gene switch, the method comprising selecting a ligand binding domain from a nuclear hormone receptor and constructing a library of transcription factors by mutating amino acid residues that hinder the binding of a selected inactive hormone analogue.

6. claims: 21,22,29,31

A compound that binds to and activates a transcription factor comprising a DNA-binding domain, a modified ligand-binding domain according to the invention and a transcription regulatory domain, a compound according to CMP1 or CMP4-38, a method for making inactive analogues of hormones.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 21 (partially)

Present claim 21 relates to a product defined by reference to a desirable characteristic or property, namely a compound that binds to and activates the transcription factor of claim 12. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds CMP1 and CMP4-38

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

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